***In re National Prescription Opiate Litigation*: MDL 2804**

Summary Sheet of Concise Issues Raised

Opposition Name: Plaintiffs' Memorandum of Law in Opposition to Defendants' Motion to Exclude "Marketing Causation" Opinions of Drs. Schumacher, Lembke, and Keyes

Opposing Parties: Plaintiffs Summit County and Cuyahoga County

Issue: Are the opinions of Drs. Schumacher, Lembke and Keyes, that Defendants' false and misleading marketing of prescription opioids was a cause of the opioid epidemic, admissible under *Daubert* and Fed. R. Evid. 702?

***Answer*:** Yes. Defendants move to exclude what they call "marketing causation" opinions offered by Drs. Mark Schumacher, Anna Lembke, and Katherine Keyes, arguing that these witnesses are not qualified to offer opinions about marketing. The motion should be denied in its entirety, because Drs. Schumacher, Lembke, and Keyes are exceedingly well-qualified to opine (a) that Defendants' representations about opioids falsely downplayed the risk of addiction while exaggerating purported benefits; (b) that these misrepresentations and omissions caused doctors to prescribe opioids without proper awareness of the enormous risks and lack of benefits; and (c) that the misconceptions about opioids promoted by the Defendants were a cause of the opioid epidemic. This testimony falls squarely within the expertise of Dr. Lembke, an addiction medicine physician who performed extensive research into the opioid epidemic long before she was engaged as an expert; Dr. Schumacher, a physician who was one of 18 renowned medical and scientific experts selected by the National Academies of Sciences, Engineering and Medicine (NASEM) to assess the opioid epidemic and its causes; and Dr. Keyes, a professor of epidemiology who specializes in the epidemiology of substance use and substance use disorders. These doctors have the expertise to assess the truth, falsity, and completeness of what Defendants said about opioids; the effects on the medical profession and on prescribing of those statements; and the causes of the opioid epidemic that followed.

Defendants' brief ignores Plaintiffs' experts' pre-litigation research and published opinions. In 2017, Dr. Schumacher and the NASEM Committee stated that "heavy promotion of opioid prescribing by drug manufacturers (including misleading claims by some) and substantially increased prescribing by physicians were key contributors to the increase in misuse, OUD, and accompanying harms." In 2016, Dr. Lembke researched and published a book finding that "doctors were duped" into overprescribing by the false messages that Defendants promoted. In 2013, Dr. Keyes wrote a peer-reviewed article stating that "aggressive marketing" contributed to the opioid epidemic. All of these opinions were stated before Plaintiffs' experts had any connection to the litigation. *See Johnson v. Manitowoc Boom Trucks, Inc.*, 484 F.3d 426, 434 (6th Cir. 2007) ("That an expert testifies based on research he has conducted independent of the litigation provides important, objective proof that the research comports with the dictates of good science").

The opinions of these experts are supported by a substantial body of independent research. For example, a 2018 article concluded that "overwhelming evidence of misinformation and misdeeds" by drug manufacturers and distributors were among the causes of the opioid epidemic; a 2009 article found that Defendants had overstated the benefits of the drugs while falsely claiming that the risk of addiction was extremely small (Pl. Opp. Br. at 7-9). The review of scientific literature is a sound methodology. *In re Gadolinium-Based Contrast Agents Products Liab. Litig.*, No. 1:08 GD 50000, 2010 WL 1796334, *mod. on recon.*, 2010 WL 5173568, *aff'd sub nom. Decker v. GE Healthcare Inc.*, 770 F.3d 378 (6th Cir. 2014) (finding expert testimony based on review of scientific literature

admissible); *see also*, *In re Heparin Prods. Liab. Litig.*, 803 F. Supp. 2d 712738 (N.D. Ohio 2011) ("Courts have admitted expert testimony as reliable where experts extrapolate their opinions from their knowledge and experience combined with a review of the relevant scientific literature.")

The proposed testimony of Drs. Lembke, Schumacher, and Keyes applies reliable methodology, including reliance on their own pre-litigation research and peer-reviewed scientific literature. Their opinions will assist the trier of fact and should not be excluded.

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UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

IN RE NATIONAL PRESCRIPTION OPIATE LITIGATION	MDL 2804
	Case No. 17-md-2804
This document relates to:	Hon. Dan Aaron Polster
Track One Cases	

PLAINTIFFS' MEMORANDUM IN OPPOSITION TO DEFENDANTS' MOTION TO EXCLUDE "MARKETING CAUSATION" OPINIONS OF DRS. SCHUMACHER, LEMBKE AND KEYES

July 31, 2019

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INTRODUCTION

Defendants move to exclude what they call "marketing causation" opinions offered by Drs. Mark Schumacher, Anna Lembke, and Katherine Keyes, arguing that these witnesses are not qualified to offer opinions about marketing. The motion should be denied in its entirety, because Drs. Schumacher, Lembke, and Keyes are exceedingly well-qualified to opine (a) that Defendants' representations about opioids were false and misleading, and omitted important material information; (b) that these fraudulent misrepresentations and omissions caused doctors to prescribe opioids without proper awareness of the risks and without adequate safeguards against those risks; and (c) that the misconceptions about opioids promoted by the Defendants were a cause of the opioid epidemic. This testimony falls squarely within the expertise of Dr. Lembke, an addiction medicine physician who performed extensive research into the opioid epidemic long before she was engaged as an expert; Dr. Schumacher, a physician who was one of 18 renowned medical and scientific experts selected by the National Academies of Sciences, Engineering and Medicine (NASEM) to assess the opioid epidemic and its causes; and Dr. Keyes, a professor of epidemiology who specializes in the epidemiology of substance use and substance use disorders. These doctors have the expertise to assess the truth, falsity, and completeness of what Defendants said about opioids; the effects on the medical profession and on prescribing of those statements; and the causes of the opioid epidemic that followed.

Defendants' attacks on the methodology and reliability of the experts' opinions are similarly unfounded. The opinions of these experts are supported by epidemiological and scientific evidence, including a substantial body of independent research that predates this litigation. Their conclusion -- that misrepresentations about the risks and benefits of opioids led to the epidemic of addiction and associated ills -- is both well-supported and widely accepted. The proposed testimony of

Drs. Lembke, Schumacher, and Keyes is grounded in reliable science, applies reliable methodology, will assist the trier of fact, and should not be excluded.

LEGAL STANDARD

The legal standards applicable to this motion are set forth in Plaintiffs' *Daubert* Roadmap Brief, to which the Court is respectfully referred.

ARGUMENT

I. PLAINTIFFS' EXPERTS ARE QUALIFIED TO OFFER THE OPINIONS IN THEIR REPORTS

Defendants argue that Drs. Lembke, Schumacher, and Keyes are not qualified to offer the opinions in their reports, but this argument rests on mischaracterizations about their expertise and about the opinions they offer. Thus, Defendants characterize Mark Schumacher, M.D., as "an anesthesiology professor with a Ph.D. in physiology and pharmacology," (Defs. Dkt. # 1868-2, at 4), while omitting Dr. Schumacher's most relevant and significant credential in this litigation: Dr. Schumacher was one of 18 renowned medical and scientific experts, selected by NASEM to assess the opioid epidemic and issue a report with recommendations on how to remedy the problems created by that epidemic.[1] The NASEM Committee reached a consensus that Defendants' marketing contributed causally to the opioid epidemic, and Dr. Schumacher's work on that panel reliably supports his opinions. Dr. Schumacher was not retained as an expert consultant until 2019, over a year after his opinions were a matter of public record.[2] Of particular relevance to this Motion, the NASEM Report stated that, despite FDA's instruction to the panel that its task was not to assign blame for the current situation, "*certain hypotheses about causes of the epidemic are inescapable.* For example, the data presented earlier in this chapter make a prima facie case that *heavy promotion of opioid prescribing by drug manufacturers (including misleading claims by some)* and substantially increased prescribing

[1] Ex. 1, Nat'l Acads. of Scis., Eng'g & Med. (NASEM), *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use* at v-vi (The Nat'l Acads. Press 2017).

[2] *Id.*

by physicians were key contributors to the increase in misuse, OUD, and accompanying harms."[3] Also, Committee members' financial conflicts of interest, if any, were listed in the Biographical Sketches in the NASEM Report; Dr. Schumacher had no conflicts to disclose.[4] The argument that Dr. Schumacher lacks the expertise to assess the causes of the opioid epidemic is frivolous.

Similarly, Plaintiffs' expert Anna Lembke, M.D., is qualified by experience and her own pre-litigation research to offer opinions about the causes of opioid epidemic. *See* Fed. R. Evid. 702. Dr. Lembke is Chief of the Addiction Medicine Dual Diagnosis Clinic, Medical Director of Addiction Medicine, and Program Director of the Addiction Medicine Fellowship, in the Department of Psychiatry and Behavioral Sciences at Stanford University School of Medicine. She is Board-certified in psychiatry and neurology, and in addiction medicine. She regularly treats patients with addiction to opioids and other substances; for the last 15 years, her clinical practice has included a significant proportion of patients taking prescription opioids for pain relief, for whom such drugs have resulted in misuse, dependence, and addiction.

Of perhaps greater significance in this context, in 2016 (before she had any connection to this litigation), Dr. Lembke published her influential book, *Drug Dealer, MD: How Doctors Were Duped, Patients Got Hooked, and Why It's So Hard to Stop*, in 2016. *See Johnson v. Manitowoc Boom Trucks, Inc.*, 484 F.3d 426, 434 (6th Cir. 2007) ("[A]n expert testifies based on research he has conducted independent of the litigation provid[ing] important, objective proof that the research comports with the dictates of good science . . . .") (citation omitted). In that book, Dr. Lembke described the "misconceptions" promoted by Defendants through their financial support for Key Opinion Leaders and professional medical societies like the American Pain Foundation (principally, unsupported claims of efficacy for chronic pain, and purportedly low risk of addiction) that gave rise to the opioid epidemic; Dr. Lembke's expert witness Report cites the same misconceptions that she

[3] *Id.* at 40-41 (emphasis added).

[4] *Id.* at 436-46.

had reported in the book she wrote prior to litigation, further supported by her review of Defendants' internal documents.[5] Dr. Lembke's Report also relied on the NASEM text quoted above, in support of her opinion that the "nearly quadrupling of opioid prescribing between 1999 and 2012 does not merely correlate with rising rates of opioid addiction and related deaths. It is causative."[6] By the time her book was published, if not before, Dr. Lembke had developed substantial expertise in these areas.

Dr. Katherine Keyes is an Associate Professor of Epidemiology at Columbia University, specializing in substance use and substance use disorders epidemiology.[7] Epidemiology is the "science of understanding the causes and distributions of population health" and "epidemiologists examine the dynamic nature of populations and how health and disease arises within them."[8] By definition, epidemiology plays a role in describing the opioid epidemic and its causes, and Dr. Keyes is, accordingly, qualified to opine on this topic. In addition, Dr. Keyes has extensive expertise on opioid-related harm, including large scale survey data and vital statistics analyses, as well as the development of theories, hypotheses, and published findings concerning the role of macro-social factors in producing the opioid epidemic.[9] She has published 19 peer-reviewed journal articles on opioid use and related harms (and many more on drug use disorders generally), detailing trends over time in prescription opioid misuse, birth cohort trends in nonmedical opioid use and overdose, risk factors for non-medical prescription opioid use, and consequences of use across developmental periods, including consequences related to overdose.[10] For example, Dr. Keyes reported in a 2013

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[5] *Compare* Report of Anna Lembke, MD, Dkt. # 2000-10 ¶¶ B.4.a-d, at 5 (summarizing opinions attributing the opioid epidemic to industry-promoted "misconceptions" that are detailed throughout the Report) with her book Ex. 2, Anna Lembke, *Drug Dealer, M.D.: How Doctors Were Duped, Patients Got Hooked and Why It's So Hard to Stop* 57-64 (Johns Hopkins Univ. Press 2016), which recounts the same "misconceptions" of efficacy for chronic pain; no dose is too high; addiction is rare; and the concept of "pseudoaddiction."

[6] Lembke Rep., Dkt. # 2000-10 ¶ C.5.a., at 37.

[7] Report of Katherine Keyes, Dkt. # 2000-9 at 1.

[8] *Id.* at 7.

[9] *Id.* at 2.

[10] *Id.* at 2.

article that "steps in the 1990s to increase the availability and use of analgesics, including aggressive marketing of potent formulations such as oxycodone hydrochloride and efforts to encourage clinicians to be more proactive in identifying and treating chronic pain," contributed to the opioid epidemic.[11]

As the above descriptions show, Plaintiffs' experts are well-qualified to offer opinions that Defendants' marketing of prescription opioids was false and misleading in its overstatement of benefits and understatement of risks, and that such promotion was a cause of the overprescribing that gave rise to the epidemic. It is well-established that witnesses with medical and scientific expertise are permitted to offer opinions that a pharmaceutical defendant's promotional statements are inadequate to accurately convey the risks and benefits of their product. *See, e.g.*, *In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Prods. Liab. Litig.*, No. MDL 1203, 2000 WL 876900, at *11 (E.D. Pa. June 20, 2000). "In other words, [plaintiffs' experts] are qualified to render an opinion as to the labels' completeness, accuracy, and—it follows from that—the extent to which any inaccuracies or omissions could either deprive a reader or mislead a reader of what the risks and benefits of the [drug] in issue are or were at the time the labeling was published." *Id.*; *In re Gadolinium-Based Contrast Agents Prods. Liab. Litig.*, MDL 1909, No. 1:08-GD-50000, 2010 WL 1796334, at *19 (N.D. Ohio May 4, 2010) (Polster, J.) ("[Plaintiffs' expert] may offer opinions on whether Omniscan's labeling information or Dear Doctor letters contained adequate information, or inaccuracies or omissions that could deprive or mislead physicians like himself who treat renally impaired patients about the risks associated with Omniscan administration."). It is equally well-established that an expert can be qualified under Rule 702 based on experience. Fed. R. Evid. 702 ("A witness who is qualified as an expert by knowledge, skill, experience, training, or education may

[11] Ex. 3, M. Cerda, *et al.*, *Prescription Opioid Mortality Trends in NYC, 1990-2006*, 132 Drug Alcohol Dependency 1-21, 10 (2013).

testify in the form of an opinion or otherwise . . . ."); *United States v. Mallory,* 902 F.3d 584, 592 (6th Cir. 2018). Plaintiffs' experts are qualified in all respects.

II. PLAINTIFFS' EXPERTS APPLIED A RELIABLE METHODOLOGY TO SUPPORT OPINIONS THAT DEFENDANTS' MISLEADING CLAIMS ARE A CAUSE OF THE OPIOID EPIDEMIC

Defendants attack the methodology used by Drs. Lembke, Schumacher, and Keyes, on four grounds. They contend that the absence of statistical analysis renders the opinions inadmissible; that the absence of physician or patients interviews in Summit and Cuyahoga Counties means that their methodologies were flawed; that the experts failed to consider alternative causes; and that they did not consider the impact of specific marketing materials. None of these criticisms holds up. Moreover, Defendants' motion ignores entirely the substantial indicia of reliability that establish the admissibility of these opinions.

A. The Experts' Opinions Are Based on a Reliable Methodology, Are Supported by Authoritative Texts and Peer-Reviewed Literature, and Were Formed Prior to Their Involvement in This Litigation

The opinions at issue here were formed through a reliable methodology: review and assessment of relevant scientific literature and the facts of the case, in light of the witness's training and experience. It is well-established that this kind of review and assessment of scientific literature is a reliable methodology. *See, e.g.*, *Smith v. Pfizer Inc.*, 714 F. Supp. 2d 845, 856 (M.D. Tenn. 2010) (finding expert's reliance on and frequent cites to scholarly articles and studies to be a reliable methodology).[12] Plaintiffs' experts reviewed the evidence and the literature applicable to the Defendants' promotion of opioid drugs, concluded that the promotion was false and misleading,

[12] *Ferguson v. Lear Siegler Servs., Inc.*, No. 1:09CV635-MHT, 2012 WL 1058983, at *5 (M.D. Ala. Mar. 28, 2012) (finding the evidence the expert relied on in reaching his conclusion (a combination of peer-reviewed articles and experimentation conducted by others) is reliable and he applied it in a manner consistent with scientific principles); *Tressler v. BNSF Ry. Co.*, No. CV-10-188-RMP, 2012 WL 315402, at *6 (E.D. Wash. Feb. 1, 2012) (finding medical and scientific literature review and evaluation of available epidemiological data is reliable methodology); *In re Avandia Mktg., Sales Practices & Prods. Liab. Litig.*, No. 2007-MD-1871, 2011 WL 13576, at *9 (E.D. Pa. Jan. 4, 2011) ("[The expert's] opinions expressed in this case are based on reliable scientific methodology (the review of peer-reviewed, published studies and data using well established statistical and scientific principles).").

and that such false and misleading promotion was a cause of the opioid epidemic, just as many other independent scientists had stated in the scientific literature. This is an inherently reliable basis for expert opinions.

As noted above, moreover, Plaintiffs' experts formed their opinions *prior* to their engagement in this case, in the ordinary course of their own professional research. Although not essential to admissibility, the development of Plaintiffs' experts' opinions based on their work prior to litigation is a strong indicator of reliability. *See Johnson*, 484 F.3d at 434 ("That an expert testifies based on research he has conducted independent of the litigation provides important, objective proof that the research comports with the dictates of good science . . . .") (citation omitted); *Mike's Train House, Inc. v. Lionel, L.L.C.*, 472 F.3d 398, 408 (6th Cir. 2006); *Nelson v. Tenn. Gas Pipeline Co.*, 243 F.3d 244, 252 (6th Cir. 2001); *see also Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 152 (1999) (purpose of gatekeeper role is to ensure that expert "employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field").

The experts' opinions are, moreover, supported by a large body of well-accepted scientific evidence. In addition to the above-mentioned independent opinions reached by Plaintiffs' experts prior to litigation, multiple scientific articles, written over a period of many years, support Plaintiffs' expert opinions that Defendants' misleading promotion of prescription opioids was causally related to the epidemic of opioid-induced addiction and mortality. For example, a 2018 article published in *Pain Physician* was authored by several influential medical doctors affiliated with pain management centers, none of whom identified as "marketing" experts.[13] These physicians cited "*overwhelming evidence of misinformation and misdeeds by drug manufacturers*, drug dealers, *drug distributors*, and multiple

[13] Dr. Manchikanti, the lead author, is Chairman of the Board and Chief Executive Officer, American Society of Interventional Pain Physicians, with over 490 published articles in the field of pain medicine. *See* Ex. 4, Pain Mgmt. Ctrs. of Am., https://www.thepainmd.com/manchikanti (last visited July 28, 2019). None of the authors of the 2018 article declared any financial conflicts of interest.

agencies overseeing controlled substance activities" among the causes of the opioid epidemic.[14] This lengthy review described the "confluence of the emergence of the influence of pharma and the death of evidence-based medicine;" the observation that "OxyContin was falsely marketed as an opioid with low addiction potential;" a "large, aggressive sales force" promoting prescription opioids; advocating the concept of "pseudo-addiction," which increased usage of opioids among patients who displayed drug-seeking behavior more indicative of addiction itself; and manipulation of State Medical Boards through industry funding of the Pain Policy Studies Group, to remove sanctions on opioid prescribing, while encouraging the concept of pain as the "5th vital sign."[15] Indeed, the authors conclude that one of the significant factors resulting in the epidemic was "the influence of greed-based advocacy on the pain movement."[16] The history recounted by these independent authors in a scientific journal closely mirrors the opinions stated by Plaintiffs' experts, based on the same set of facts, and their article is among the materials relied upon by Dr. Lembke.[17] Plaintiffs' experts' opinions on the effect of Defendants' aggressive, false and misleading promotion of opioids are strongly supported by the scientific literature and based on reliable sources.

Numerous additional studies in scientific journals reach similarly supportive conclusions. A 2010 "Perspective" in the *New England Journal of Medicine* ("NEJM") found that "escalations" in substance abuse and mortality "parallel[ed] an increase by a factor of 10 in the medical use of opioids since 1990, spurred in part by *aggressive marketing of OxyContin*, an extended release form of oxycodone approved in 1995, and by *efforts to encourage clinicians to become more proactive in identifying and treating chronic pain.*"[18] As detailed in Dr. Lembke's Report, and as documented in the *Pain Physician*

[14] Ex. 5, L. Manchikanti, *et al.*, *Reframing the Prevention Strategies of the Opioid Crisis*, 29 Pain Physician 309-326, 313 (2018) (emphasis added).

[15] *Id.* at 314.

[16] *Id.* at 322-23.

[17] Lembke Rep., Dkt. # 2000-10 at Ex. B, Materials Considered #244 at 19.

[18] Ex. 6, S. Okie, *A Rising Tide of Opioids, a Flood of Deaths*, 363 New Eng. J. Med. 1981-1985, 1982 (2010) (emphasis added); *see also* Lembke Rep., Dkt. # 2000-10 at Ex. B, Materials Considered #291 at 22.

2018 article (above), those efforts to encourage clinicians to be "proactive" were surreptitiously funded by the Defendants themselves, further supporting the causal link between aggressive marketing, increased sales, and the epidemic of addiction and mortality.[19] The NEJM article further quotes an FDA Advisory panel member who stated that prescription opioids "are essentially legal heroin."[20]

Van Zee's peer reviewed 2009 article documented the evidence that Purdue's marketing of OxyContin overstated the benefits of the drug while falsely claiming that the risk of addiction was extremely small; that Purdue targeted physicians with "educational" sessions and merchandise to encourage prescribing; that free starter prescriptions probably exacerbated the epidemic of abuse and increased mortality; and that OxyContin's "success, fueled by an unprecedented promotion and marketing campaign, was stained by escalating OxyContin abuse and diversion that spread throughout the country."[21]

A 2007 epidemiologic analysis by a CDC official concluded: "The upward trend in drug-induced mortality since 1990 is *largely due to the increasing numbers of deaths associated with prescription drugs* rather than illegal drugs. Prescription drugs now contribute to more unintentional drug-induced deaths in the US than illegal drugs. This upturn in unintentional drug deaths owes a great deal to the *dramatic increases in prescribing of, and overdoses from, opioid analgesics since 1990.*"[22] An Ohio Department

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[19] *See* Lembke Rep., Dkt. # 2000-10 at App. II, Summary of Documents from the University of Wisconsin Pain and Policy Study Group at 5, wherein Dr. Lembke summarizes the funding of such efforts by Purdue, Janssen, Endo, Ortho-McNeil, Cephalon, Alpharma, Abbott, *et al.*, concluding: "These documents provide supportive evidence for my opinion that one of the ways that the Pharmaceutical Opioid Industry created the opioid epidemic in the United States was by funding the PPSG to 'educate' the medical community as to the 'necessity' for such drugs, to influence state legislatures to increase access while loosening restrictions on prescribing, and to change the very culture of opioid prescribing, by suggesting that failing to prescribe opioids was tantamount to 'undertreating' pain and violating a patient's 'rights.'"

[20] Ex. 6, Okie, *supra*, note 18, at 1981.

[21] Ex. 7, A. Van Zee, *The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy*, 99 Am J Public Health 221-227, 225 (2009).

[22] Ex. 8, L.J. Paulozzi, *et al.*, *US Data Show Sharply Rising Drug-Induced Death Rates*, 13 Injury Prevention 130-132, 130-131 (2007) (emphasis added). Paulozzi was identified in the article as affiliated with the Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, of the CDC. *See also* Lembke Rep., Dkt. 2000-10 at Ex. B, Materials Considered # 306 at 23.

of Health, Violence and Injury Prevention Program document citing statistical data through 2008, stated that the increase in the Ohio drug poisoning death rate from 1999-2008, was "largely driven by prescription drug overdoses;" that prescription opioids "are associated with more overdoses than any other prescription or illegal drug including cocaine and heroin;" that "[t]here is a strong relationship between increases in sales of prescription opioids and fatal unintentional drug poisoning rates;" that a 304% increased unintentional poisoning death rate closely correlated with a 325% increase in total grams of prescription opioids distributed per 100,000 population, from 1999-2007; and that "*Changing medical and advertising practices*," including marketing directly to consumers, were among the causes for the increased death rate.[23] The promotional materials cited in the Appendices to Dr. Lembke's Report provide additional, consistent evidence supporting her opinions, based on Defendants' internal documents that are not in the public domain and would not have been available to her previously.[24]

In short, there has been widespread, authoritative and peer-reviewed endorsement of the conclusion that Defendants' aggressive and misleading promotion of prescription opioids is the root cause of the opioid epidemic. To counter this, Defendants seek to impose their own specific requirements on what constitutes a sufficient basis for Plaintiffs' experts' testimony. However, there is no prescribed methodology that experts must follow to develop their opinions. *See Buck v. Ford Motor Co.*, 810 F. Supp. 2d 815, 844 (N.D. Ohio 2011) ("[A]n expert need not actively conduct his or her own tests to have a valid methodology.") (citation and internal quotation marks omitted); *Kumho*, 526 U.S. at 139 ("[W]hether *Daubert's* specific factors are, or are not, reasonable measures of reliability in a particular case is a matter that the law grants the trial judge broad latitude to

[23] Ex.9, CUYAH_001709667-CUYAH_001709674. The document also noted, at CUYAH_001709671: Over 300% increase in admissions for non-heroin substance abuse treatment in the past decade (through 2008); and at CUYAH_001709672: "In addition to the tragic loss of human life, drug overdoses are associated with high direct and indirect costs. Unintentional fatal poisonings cost Ohioans $3.5 billion each year, while non-fatal, hospital admitted poisonings cost an additional $31.9 million." (Includes medical costs, loss of work, and quality of life loss.)

[24] *See* Lembke Rep., Dkt. # 2000-10 at Appendices I and II, providing examples of Defendants' false and misleading promotion.

determine."). "Experts are permitted wide latitude in formulating their opinions . . . ." *In re E. I. du Pont de Nemours & Co. C-8 Pers. Injury Litig.*, 345 F. Supp. 3d 897, 911 (S.D. Ohio 2015) (citing *Jahn v. Equine Servs., PSC*, 233 F.3d 382, 388 (6th Cir. 2000)). Defendants are not empowered to dictate the methodology to be employed by Plaintiffs' experts, and their critiques do not withstand scrutiny.

B. "Statistical Analysis" Is Not Essential to Opinions that False and Misleading Promotion Was a Cause of the Opioid Epidemic

Defendants argue that the opinions of Lembke, Schumacher and Keyes are "unreliable" because they did not conduct "statistical analysis" to determine the effect of Defendants' marketing. However, Defendants cite no cases holding that a statistical analysis is required to support their opinions. To the extent that a statistical analysis is required, Plaintiffs' experts have opined that there was a clear and obvious correlation between increased sales of prescription opioids and increased mortality, and that this was more than mere coincidence. *See, e.g.*, Lembke Report, providing extensive statistical data to demonstrate "prolific" increased opioid prescribing from the 1990s forward, including longer duration and higher dose prescriptions, "distributed across different types of prescribers"[25]); statistical data showing the increased risk of opioid use disorder with those higher doses and longer durations[26]; data showing the "clear link" between "increased opioid prescribing," and greater exposure to higher doses and for longer durations, "contributing to rising incidence and prevalence of opioid misuse, dependence and addiction"[27]; statistical data documenting the increased numbers of deaths and non-fatal overdoses during the epidemic[28]; data specifically showing the increased prescriptions in the bellwether counties, in absolute terms and in relation to national averages[29]; and the conclusion that the "misconceptions" promoted by Defendants "were the single most significant factor giving rise to the massive increase in the sale of

[25] Lembke Rep., Dkt. # 2000-10 ¶ C.2, at 9-13.
[26] *Id.* at ¶¶ C.3.a.iv-v, at 15.
[27] *Id.* at ¶¶ C.5.c.i-iv, at 38-39.
[28] *Id.* at ¶¶ C.11-14, at 81-88.
[29] *Id.* at ¶¶ C.2.d.i-iv, at 13.

opioids and the resulting epidemic of dependence and addiction, as detailed in [Dr. Lembke's] Report."[30] The data cited by Dr. Lembke are derived from reliable sources, including the Centers for Disease Control and Prevention and dozens of peer-reviewed articles.[31]

C. In Light of the Overwhelming Evidence that Defendants' Marketing Schemes Contributed To Wide-Spread Availability of Opioids, Physician Interviews Are Unnecessary

It is axiomatic that the purpose of pharmaceutical companies' marketing initiatives is to increase prescriptions and sales. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2008 WL 2696916, at *33 (E.D.N.Y. July 2, 2008), *opinion clarified,* No. 04-MD-1596, 2008 WL 2705475 (E.D.N.Y. July 9, 2008) ("It is undisputable that expenditures for drug marketing increase sales. The billions spent by the pharmaceutical industry attests to that. Physicians, despite what most claim, *are* influenced both consciously and unconsciously by commercial promotional messages."). As part of Dr. Keyes's analysis, she found "[e]vidence shows that pharmaceutical marketing of prescription drugs increases prescribers' likelihood of prescribing the marketed drug in the future . . . ."[32] Here, Defendants' successful marketing campaigns increased distribution of prescription opioids from 1997 to 2007 by more than 600%.[33] This increased supply resulted in "the widespread availability of prescription opioids that were originally dispensed for medical uses, often in greater quantities and doses than needed, leaving a surplus of opioids that could be diverted for non-medical uses."[34] Dr. Keyes explains that this is not a new phenomenon and that the

[30] Lembke Rep., Dkt. # 2000-10 ¶ C.10, at 75.

[31] Plaintiffs note as well that their expert Meredith Rosenthal *did* perform a statistical analysis linking Defendants' marketing to increased sales of opioids. Report of Meredith Rosenthal, Dkt. # 2000-23.

[32] Keyes Rep., Dkt. # 2000-9 at 11 (*citing* Ex. 10, F. Fickweiler, *et al.*, *Interactions Between Physicians and the Pharmaceutical Industry Generally and Sales Representatives Specifically and Their Association with Physicians' Attitudes and Prescribing Habits: a Systematic Review*, 7 BMJ Open. 1-12 (2017); Ex. 11, C. DeJong C, *et al.*, *Pharmaceutical Industry–Sponsored Meals and Physician Prescribing Patterns for Medicare Beneficiaries*, 176 JAMA Intern Med. 1114-22 (2016)).

[33] Keyes Rep., Dkt. # 2000-9 at 10 (*citing* Ex. 12, L.J. Paulozzi, *et al.*, *CDC Grand Rounds: Prescription Drug Overdoses—a U.S. Epidemic*. 61 Morb Mortal Wkly Rep. 10-13 (2012); Ex. 13, US Dep't of Justice; Drug Enforcement Admin., Automation of Reports and Consolidated Orders Sys. (ARCOS), https://www.deadiversion.usdoj.gov/arcos/index.html (last visited July 28, 2019)).

[34] Keyes Rep., Dkt. # 2000-9 at 20 (*citing* Ex. 14, S.S. Martins, *et al.*, *Birth-Cohort Trends in Lifetime and Past-Year Prescription Opioid-Use Disorder Resulting From Nonmedical Use: Results From Two National Surveys*, 71 J. Stud. Alcohol Drugs. 480-87

"relationship between supply of an addictive substance and subsequent rates of substance use disorder has been well established in the public health literature for years, under the model of 'availability theory.'"[35] This relationship has been "extensively documented for decades for alcohol and tobacco, and is one reason that alcohol and cigarette taxes, minimum pricing, and other public health efforts aimed at availability and price are among the most effective population level interventions to reduce" harm.[36]

Scientific and medical literature, including the NASEM Report, concludes that Defendants' successful marketing resulted in wide-spread availability of opioids, and that there was a close link between over-supply and the numbers of opioid-related deaths, which supports Plaintiffs' experts' conclusions. In particular, Dr. Keyes noted that there was significant variation in opioid prescribing between different states, and that the extent of opioid prescribing correlated closely with the extent of increased prescription opioid overdose in each state;[37] such a correlation is strongly supportive of a causal link between the success of the marketing, the extent of sales, and the number of deaths.

Moreover, as the First Circuit has noted, it is well-recognized that asking doctors individually what influenced their prescribing is unreliable. *See In re Neurontin Mktg. & Sales Practices Litig.*, 712 F.3d 21, 30 (1st Cir. 2013). This is especially true in the context of controversial prescribing patterns where "self-reporting from physicians . . . shows both conscious reluctance and unconscious bias, which lead them to deny being influenced." *Id.* Aggregate data, such as that relied on in the articles reviewed by the experts at issue here, provides a more reliable indication than individual physician anecdotes.

(2010); Ex. 15, E.H. Crane, *Emergency Department Visits Involving Narcotic Pain Relievers,* CBHSQ Rep. (2015), among other articles)).

[35] Keyes Rep., Dkt. # 2000-9 at 29.

[36] *Id.* at 29.

[37] *Id.* at 21.

Thus, Defendants' reliance on *In re Rezulin Products Liability Litigation*, 309 F. Supp. 2d 531, 555–56 (S.D.N.Y. 2004) and *In re Actos® (Pioglitazone) Products Liability Litigation*, No. 6:11-MD-2299, 2014 WL 12653759, at *13 (W.D. La. Jan. 14, 2014), for the proposition that Plaintiffs' experts cannot know how Defendants' marketing scheme impacted physician prescribing, is misplaced. Plaintiffs' experts in this case rely on objective data and peer-reviewed literature that show a substantial increase in prescription distribution and sales, accompanied by proportionately increased mortality, as summarized above.[38] No similar evidence was present in the *Rezulin* or *Actos* cases.[39]

D. Plaintiffs' Experts Considered Alternative Causes

Defendants also argue that Plaintiffs' experts have not considered alternative possible causes of the prescription opioid epidemic. This is demonstrably false. Dr. Lembke's report, for example, explicitly states that "others," besides the Pharmaceutical Opioid Industry, "had some responsibility for the events that have transpired," and the roles of such other contributors are summarized in her Report.[40] Similarly, Dr. Schumacher considered alternative explanations for the epidemic, as Defense counsel elicited at his deposition, where Dr. Schumacher testified, "if you look at most of these, a society disproportionally fearful or patient satisfaction surveys, or lack of formal education on pain, none of these independently would, in my opinion, have generated an opioid epidemic without the introduction and promotion, aggressive promotion of opioid analgesics in the use of chronic noncancer pain."[41] Dr. Keyes likewise assessed alternative causes, such as economic conditions or despair/depression.[42] She opined that the data on depression across time and the

[38] *Id.* at 10 (citing Ex. 12, Paulozzi, *supra*, note 33; Ex. 13, U.S. Dep't of Justice, *supra* , note 33).

[39] See also, Pls.' Br. in Opp'n to Defs.' Mot. to Exclude "Gateway" Opinions of Drs. Lembke, Gruber & Keyes, summarizing Professor Gruber's opinion that increased mortality was causally related to the amount of opioids shipped to particular geographic regions, based on regression analyses that excluded other possible explanations for the higher death tolls. Professor Gruber's analysis is parallel to that of Drs. Lembke, Keyes and Schumacher, and these opinions are mutually supportive.

[40] Lembke Rep., Dkt. # 2000-10 ¶¶ C.10.e.i-iii, at 78-80.

[41] Mark A. Schumacher Dep. (4/23/2019), Dkt. # 1970-18 at 161:3-13.

[42] Keyes Rep., Dkt. # 2000-9 at 28.

available evidence from economic studies reveal economic conditions played a relatively small part in increased opioid-related morbidity and mortality, and that the driving force "was access to and wide-spread availability of opioids."[43]

Plaintiffs' experts reliably opined that increased exposure paired with increased mortality provide persuasive evidence of a causal association, rather than a coincidence, just as the authors of the NASEM Report and numerous peer reviewed scientific articles have done. Any contributions to the epidemic from other factors go to the weight of the Plaintiffs' experts' opinions, and not their admissibility. *See Best v. Lowe's Home Ctrs., Inc.*, 563 F.3d 171, 181–82 (6th Cir. 2009).

E. The Experts Need Not Consider Each Defendant Separately in Order to Offer Opinions about the Collective Effect of Their Marketing

Defendants' argument about consideration of individual defendant marketing goes to the sufficiency, not the reliability or the admissibility, of the expert opinions. Drs. Lembke, Schumacher, and Keyes opine about the connection between the Defendants' conduct and the opioid epidemic. As discussed above, their opinions are based on a reliable methodology, grounded in good science, and supported by a wealth of scientific literature. No more is required for them to be admissible.

Whether the opinions of these experts – who do not purport to opine about particular defendants – is sufficient to establish liability of particular defendants is beyond the scope of the Court's gatekeeping function under Rule 702 and *Daubert*. *See Monroe v. FTS USA, LLC*, 860 F.3d 389, 401 (6th Cir. 2017) (differentiating challenge to sufficiency from challenge to admissibility); *Hirsch v. CSX Transp., Inc.*, 656 F.3d 359, 362 (6th Cir. 2011) (expert opinion may be admissible but insufficient); *In re Heparin Prods. Liab. Litig.*, 803 F. Supp. 2d 712, 724 (N.D. Ohio 2011) (admissibility considered on *Daubert* motion; sufficiency on motion for summary judgment), *aff'd sub nom. Rodrigues v. Baxter Healthcare Corp.*, 567 F. App'x 359 (6th Cir. 2014). The opinions of these

[43] *Id.* at 27-28 (citing multiple articles).

experts are not Plaintiffs' sole evidence of causation; thus, they need not be sufficient, on their own, to satisfy any particular element of Plaintiffs' claims, so long as they are relevant and will assist the trier of fact. Moreover, the question of the sufficiency of Plaintiffs' causation evidence, including the evidence of Drs. Lembke, Schumacher, and Keyes, but also including the evidence of Plaintiffs' economists experts, as well as Defendants' own documents establishing the effectiveness of their marketing, is the subject of Plaintiffs' responses to Defendants' summary judgment motions on this issue, including Plaintiffs' Memorandum of Law in Opposition to Manufacturers' Brief in Support of Motion For Summary Judgment For Plaintiffs' Failure to Offer Proof of Causation and Plaintiffs' Memorandum of Law in Opposition to Distributor Defendants' Motion for Summary Judgment on Proximate Cause, to which the Court is respectfully referred.

F. The Cases Cited by Defendants Do Not Support Their Motion

None of the cases Defendants cite are remotely similar to the circumstances of this litigation and none provides support for exclusion of the opinions at issue here. Defendants first cite *Rheinfrank v. Abbott Laboratories, Inc.*, No. 1:13-CV-144, 2015 WL 13022172 (S.D. Ohio Oct. 2, 2015), *aff'd*, 680 F. App'x 369 (6th Cir. 2017). In that case, the District Court ruled only that an expert without marketing or regulatory experience would not be permitted to testify "as to whether Abbott's promotion of Depakote constituted *off-label promotion*," a technical aspect of FDA regulatory law. *Id.* at *11 (emphasis added). However, the Court permitted the same expert to "opine on the medical facts and science regarding Depakote and compare that data to the Depakote label." *Id.* at *10. In this case, Plaintiffs' experts have offered opinions on the disparity between the "medical facts and science" and Defendants' labeling and other promotional statements regarding the risks and purported benefits of opioids. Such opinions were permitted in *Rheinfrank* and are admissible here. Furthermore, as noted above, a series of authoritative sources in the scientific literature support Plaintiffs' experts' opinions that the misleading and "false" information

promulgated by Defendants was a contributing cause of the epidemic, and no such circumstances existed in the *Rheinfrank* case.[44]

Defendants next rely on *Pfizer, Inc. v. Teva Pharmaceuticals USA, Inc.*, 461 F. Supp. 2d 271 (D.N.J. 2006), a patent infringement case, wherein the Court excluded expert testimony on the impact of marketing on physicians' choice among available non-steroidal anti-inflammatory drugs (NSAIDs), where the expert relied solely on "personal experience" and "common sense." *Id.* at 277.[45] As explained above, Plaintiffs' experts in this case do not rely solely on personal experience or common sense; in addition to their own experiences, they rely on authoritative sources in the scientific literature that support their opinion that Defendants' promotion of opioids contributed significantly to the resulting epidemic.[46] Also, as in *Rheinfrank,* the District Court permitted the same expert to testify that superiority claims were "misleading and falsified," by comparing "medical facts and science" to the text of the "marketing materials," quoting the ruling in the *Diet Drugs* case. *Id.* at 278.

Defendants further rely on *In re Trasylol Products Liability Litigation*, 709 F. Supp. 2d 1323 (S.D. Fla. 2010), which did not concern "marketing causation," but instead excluded an expert witness' testimony in its entirety because of a "lack of analysis or connection between the facts and the opinions persists throughout" the report and testimony at the *Daubert* hearing. *Id.* at 1350. That

[44] For these reasons, this case also differs from *In re Prempro Products Liability Litigation*, No. 4:03CV01507-BRW, 2012 WL 12906583, at *3 (E.D. Ark. Aug. 29, 2012) (excluding expert testimony that "is simply [expert's] subjective opinion on Defendants marketing materials and whatever exhibits may come in through Plaintiff's regulatory experts")

[45] Defendants likewise cite to *In re Prempro Products Liability Litigation*, 554 F. Supp. 2d 871, 882 (E.D. Ark. 2008), *aff'd in part, rev'd in part,* 586 F.3d 547 (8th Cir. 2009) for the proposition that experts cannot testify beyond their expertise, but, as explained above, Plaintiffs' experts here experience that qualified they to testify on this topic.

[46] The Court also stated that personal experience was relevant and could be considered, but that it was not sufficient in itself to support the opinions concerning the effects of promotion. *Pfizer*, 461 F. Supp. 2d at 277-78. Plaintiffs' expert Dr. Lembke included her own personal experience attending a mandatory Continuing Medical Education session that conveyed misleading information on risks and benefits to the assembled physicians (Lembke Rep., Dkt. # 2000-10, at 18), but that personal experience merely supplemented and reinforced the opinions she formed on the basis of the research she conducted in authoring a book on the subject and reviewing relevant documents and authorities.

case is not persuasive as to the issues before the Court, since Plaintiffs' experts recite extensive facts that are closely tied to their opinions and well within their expertise.

Popovich v. Sony Music Entertainment, Inc., No. 1:02 CV 359, 2005 WL 5990223 (N.D. Ohio May 9, 2005), also cited by Defendants (Defs. Dkt. # 1868-2, at 5), pertains to the valuation of a logo on a musical CD; the expert in question did not even offer marketing opinions, and the Court's opinion merely included "marketing or advertising" on a laundry list of topics about which he would not be permitted to testify. *Id.* at *3. *Popovich* is not relevant to the current motion.

In sum, the above case law relied on by Defendants does not preclude Plaintiffs' experts from testifying on the causes of the opioid epidemic in this unique matter.

III. DEFENDANTS' RULE 403 ARGUMENT SHOULD BE REJECTED

Defendants' argument that the testimony of Drs. Schumacher, Lembke and Keyes should be excluded as prejudicial under Rule 403 is simply a boilerplate argument lacking any substance. Defendants' Rule 403 argument provides no independent basis to exclude this important expert testimony and proceeds from the erroneous assumption that the testimony of Plaintiffs' experts lack any probative value because they are 'non-economists' with no marketing expertise. As explained in detail above, this is incorrect: Plaintiffs' experts are exceedingly well qualified and their testimony is based on reliable methodology supported by independent research and corroborated by epidemiological and scientific evidence. Given that the premise of Defendants' 403 argument is false, it cannot justify the exclusion of the Plaintiffs' expert testimony.

CONCLUSION

For the foregoing reasons, this Court should deny the Defendants' motion in its entirety.

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Respectfully submitted,

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